Effect of chronic renal insufficiency on outcomes of carotid endarterectomy

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Objective: **Conflicting data exist regarding the effect of chronic renal insufficiency (CRI) on carotid endarterectomy (CEA) outcomes. A large database was used to analyze the effect of CRI, defined by glomerular filtration rate (GFR), as an independent risk factor of CEA.**

Methods: **Prospectively collected data regarding CEAs performed at 123 Veterans Affairs Medical Centers as part of the National Surgical Quality Improvement Program were retrospectively analyzed. Renal function was used to divide patients into three CRI groups: normal or mild (control; GFR ≥60 mL/min/1.73 m^2), moderate (GFR 30 to 59), and severe (GFR <30). Bivariate analysis and multivariate logistic regression were used to characterize risk factors and their associations with 30-day morbidity and mortality.**

Results: **Between Jan 1, 1996, and Dec 31, 2003, 22,080 patients underwent CEA. Patients missing creatinine levels, already dialysis-dependent, or in acute renal failure just before surgery were excluded. This left 20,899 available for analysis, of which 13,965 had a GFR of ≥60, 6,423 had a GFR of 30 to 59, and 511 had a GFR of <30. The incidence of neurologic complications did not differ significantly (control, 1.7%; moderate CRI, 1.9%; severe CRI, 2.7%). The moderate CRI group experienced significantly more cardiac events (1.7% vs 0.9% for controls, $P < .001$). This remained predictive in the multivariate model even adjusting for all other risk factors (adjusted odds ratio [AOR], 1.6; 95% confidence interval [CI], 1.1-2.3; $P = .009$). The moderate CRI group also had higher rates of pulmonary complications (2.1% vs 1.3% control; $P < .001$; AOR, 1.3; 95% CI, 1.0-1.7; $P = .031$) but not 30-day mortality ($P = .269$). Those with severe CRI had a much higher mortality (3.1% vs 1.0% control, $P < .001$), which remained significant in the multivariate model (AOR, 2.7; 95% CI, 1.6-4.8; $P < .001$).**

Conclusion: **Although impaired renal function does not independently increase the risk of neurologic or infectious complications, CRI is a significant negative independent risk factor in predicting other outcomes after CEA. Patients with moderate CRI (GFR, 30-59 mL/min/1.73 m^2) are at increased risk for cardiac and pulmonary morbidity, but not death, and those with severe CRI (GFR <30 mL/min/1.73 m^2) have a much higher operative mortality. Patients with CRI should be carefully evaluated before CEA to optimize existing cardiac and pulmonary disease. Understanding this increased risk may assist the surgeon in preoperative counseling and perioperative management. (J Vasc Surg 2008;48:1423-30.)**

Stroke has been a leading cause of serious long-term disability and remains the third major cause of death in the United States even apart from other cardiovascular diseases.[1,2] Landmark trials such as the North American Symptomatic Carotid Endarterectomy Trial (NASCET), Asymptomatic Carotid Atherosclerosis Study (ACAS), and European Carotid Surgery Trial (ECST) demonstrated that in select patients with carotid stenosis, carotid endarterectomy (CEA) reduced the risk of ipsilateral stroke compared with best medical management.[3-5]

Since then, attempts have been made to identify characteristics that make certain patients high-risk for CEA.[6-13] Best medical management has undergone significant improvements with the use of β-blockers, statins, and antiplatelet agents. Determining the risk of poor outcome after CEA in individual patients is confounded by many factors, especially comorbidities.

Chronic renal insufficiency (CRI) is one risk factor that has been related to poor outcomes after CEA.[14-20] Previously published studies on this topic divided patients based on serum creatinine levels and arrived at mixed conclusions.[5,7-9,11,13-21] An explanation of the disparate results is that creatinine is a late and insensitive marker, which can remain <2.0 mg/dL despite a significant reduction of the glomerular filtration rate (GFR) to as low as 15 mL/min/1.73 m^2.[22] The inaccuracy of estimation of creatinine of total renal function is due to various factors; the National Kidney Foundation's Kidney Disease Outcome Quality Initiative (NKF KDOQI) guidelines recommend the use of GFR as a better early indicator of chronic kidney disease.[22-24]

Accordingly, it is possible that operative risks in patients with CRI have not been well estimated to date. Our objective was to analyze renal insufficiency by GFR as an independent risk factor that has a negative effect on outcomes of CEA using a large multicenter database.

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METHODS

Database. The Veterans Affairs National Surgical Quality Improvement Program (VA-NSQIP) is an ongoing quality management initiative that has been used in other outcome analysis studies. The VA-NSQIP prospectively collects quality improvement data on all operations performed at 123 participating VA medical centers in the United States.[25] Baseline clinical and demographic characteristics, operation and anesthesia information, and postoperative complication data are recorded by trained nurse reviewers from medical record review, surgeon interview, or patient follow-up, or both. Deaths are reported and verified against the VA Beneficiary Identification and Records Locator System (BIRLS) death records.

Sample selection. We queried the VA-NSQIP for all surgical encounters between Jan 1, 1996, and Dec 31, 2003, identified by the Current Procedural Terminology code 35301. All patients returned by the query were initially considered for analysis. We excluded individuals who were missing recorded serum creatinine levels, who presented in acute renal failure just before operation, or who were already dialysis-dependent. Institutional Review Board approval was obtained. All patient information was stripped of identifiers and sent to the principal investigator in a secure fashion using file encryption and password protection.

Postoperative outcomes. Primary outcomes of interest were the development of one or more postoperative complications or death ≤30 days after surgery, or both. We grouped complications into the following categories: neurologic, defined as a new cerebrovascular accident/stroke or coma lasting >24 hours; cardiac, defined as myocardial infarction or cardiac arrest; pulmonary, defined as failure to wean from the ventilator ≤48 hours or any unplanned reintubation; and infectious, defined as sepsis, urinary tract infection, or pneumonia.

Determination of renal function. In our database the serum creatinine concentration most closely preceding surgery was available for almost all patients. The abbreviated Modification of Diet in Renal Disease (MDRD) equation[26] was used to calculate GFR based on creatinine (Cr), age, gender, and race: GFR (mL/min/1.73 m^2) = 186 $\times$ (Cr)$^{-1.154}$ $\times$ (Age)$^{-0.203}$ $\times$ (0.742 if female) $\times$ (1.210 if African American).

We categorized patients into those with normal or mildly reduced renal function (GFR ≥60 mL/min/1.73 m^2), moderate renal insufficiency (GFR 30-59 mL/min/1.73 m^2), severe renal insufficiency (GFR <30 mL/min/1.73 m^2), and dialysis-dependent renal failure. We included patients with GFR <15 mL/min/1.73 m^2 in the severe renal insufficiency group as long as they were not yet actually dialysis-dependent.

These categorizations were based on the NKF KDOQI, which provides evidence-based clinical practice guidelines for all stages of chronic kidney disease and related complications.[24] Within these guidelines, all individuals with GFR <60 mL/min/1.73 m^2 for 3 months are classified as having chronic kidney disease, because this represents loss of at least half of normal adult kidney function. Though the KDOQI Work Group initially defined the above categories of severity arbitrarily, evidence compiled in later guidelines supports these cutoff levels.

Baseline patient demographic, comorbid, and operative characteristics. Various other risk factors were analyzed in addition to renal function. Patient demographics included age, sex, and race. Existing comorbidities included previous stroke/cerebrovascular accident, transient ischemic attacks (TIA), congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), diabetes mellitus (none or diet-controlled vs those requiring oral medications or insulin), American Society of Anesthesiologists (ASA) classification, and functional status. Neurologic symptoms were considered present if a patient had a history of stroke or TIA before CEA.

Preoperative functional status is defined in the VA-NSQIP as the level of self-care demonstrated ≤30 days before surgery. This is based on activities of daily living such as bathing, feeding, dressing, toileting, and walking. Patients were considered independent if they did not require assistance of nursing care, equipment, or devices.

History of cigarette smoking was quantified in pack-years and was considered current if the patient smoked ≤1 year of the operation. Current alcohol abuse was defined as the consumption of >2 drinks per day in the 2 weeks before surgery.

Basic operative characteristics were recorded, such as type of anesthesia used and duration of the operation. Preoperative laboratory values were also included on most patients, including serum albumin, hematocrit, white blood cell (WBC) count, platelet count, prothrombin time, partial thromboplastin time, and creatinine, sodium, and serum urea nitrogen levels.

Statistical analysis. Bivariate analyses were performed considering each of the risk factors, such as renal function, comorbidities, laboratory values, and operative information, against each outcome category. The Fisher exact test or the χ^2 test was used for categoric variables, and two-tailed analysis of variance (ANOVA) was used for continuous variables. All values of $P < .05$ were considered significant. If the ANOVA test was significant, a post hoc Bonferroni test was used.

For multivariate analysis, all risk factors were included in stepwise logistic regression models (with hierarchic modeling to account for clustering at the institutional level) that were generated for each outcome of interest. An entry criterion of $P < .25$ and exit/significance criterion of $P < .05$ were used to identify independent predictors. Final models were checked for goodness-of-fit using pseudo R^2 and Hosmer-Lemeshow tests. Analyses were completed using Stata 8.0 software (StataCorp LP, College Station, Tex).

RESULTS

We identified 22,080 patients who underwent CEA during the 8-year study period, of which 1070 were missing creatinine data, 76 were already dialysis-dependent, and 35

Table I. Summary of relevant baseline patient demographics, by renal function[a]

Variable	*GFR ≥60*	*GFR 30-59*	*GFR <30*
Patients, No.	13,965	6423	511
Age, mean (SD), y	66.7 (8.7)	71.5 (7.3)[b]	71.9 (7.1)[b]
Male, %	98.7	98.4	98.2
White, non-Hispanic, %	80.6	84.8[b]	80.2
History of TIA, %	33.1	31.9	32.3
History of stroke, %			
Without deficits, %	8.8	10.0[c]	9.6
With deficits, %	19.1	18.5	20.9
CHF (≤1 month pre-op), %	2.0	4.1[b]	5.7[b]
COPD (%)	15.8	17.0[d]	17.6
Diabetes mellitus, %			
Oral agent	17.3	18.1[c]	18.6[d]
Insulin, %	8.2	12.5[b]	18.0[b]
Smokers, %	44.1	31.0[b]	29.4[b]
Alcohol use, %	10.0	5.7[b]	5.3
Poor functional status, %	6.6	7.1	8.8[d]
ASA, mean (SD), class	3.06 (0.45)	3.12 (0.45)[b]	3.23 (0.47)[b]
Preoperative levels			
Albumin, mean (SD), mg/dL	3.96 (0.45)	3.90 (0.45)[b]	3.72 (0.53)[b]
WBC, mean (SD), ×1000 cells/mL	7.78 (2.53)	7.79 (2.59)	7.82 (2.32)
Hematocrit, mean (SD), %	41.5 (4.4)	39.9 (4.8)[b]	36.2 (5.2)[b]
Platelets, mean (SD), U	234 (70.9)	225 (68.9)[b]	223 (77.2)[e]
PT, mean (SD), s	12.5 (2.1)	12.6 (1.7)[e]	12.8 (1.8)

ASA, American Association of Anesthesiologists; *CHF,* congestive heart failure; *COPD,* chronic obstructive pulmonary disease; *DM,* diabetes mellitus; *GFR,* glomerular filtration rate; *PT,* prothrombin time; *TIA,* transient ischemic attack; *WBC,* white blood cells.
[a]Defined according to the estimated GFR in mL/min/1.73m^2. All statistical comparisons are made to the control group (GFR ≥60) as the reference category.
[b]$P < .001$, analysis of variance.
[c]$P < .001$, χ^2 test.
[d]$P < .05$, χ^2 test.
[e]$P < .01$, analysis of variance.

Table II. Incidence of complications after carotid endarterectomy by level of renal function[a] according to univariate analysis

Complication	*GFR ≥60 (n = 13,965), %*	*GFR 30-59 (n = 6,423), %*	*GFR <30 (n = 511), %*
Neurologic	1.7	1.9	2.7
Cardiac	0.9	1.7[b]	1.0
Pulmonary	1.3	2.1[b]	3.1[b]
Infectious	1.5	2.4[b]	4.5[b]
Death ≤30 days	1.0	1.4[c]	3.1[b]

[a]Defined by estimated glomerular filtration rate *(GFR)* in mL/min/1.73 m^2. All statistical comparisons are made to the control group (GFR ≥ 60) as the reference category.
[b]$P < .001$, χ^2 test.
[c]$P < .05$, χ^2 test.

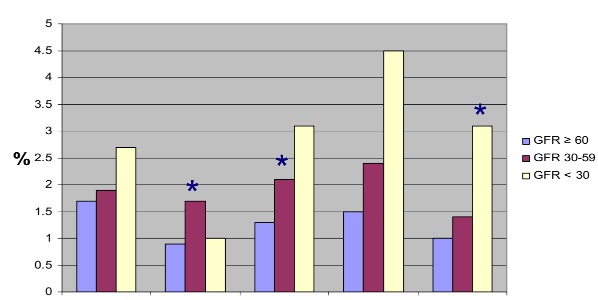

Fig. Incidence of postoperative complications after carotid endarterectomy. *Comparisons with GFR ≥60 mL/min/1.73 m^2, statistical significance in multivariate model, any $P < .05$, see Table III.

were classified in preoperative acute renal failure. Excluding these, 20,899 subjects were available for complete analysis. Characteristics of the three renal function groups are outlined in Table I. Those with CRI were statistically more likely to be older, diabetic, of higher ASA category, and have other medical problems like CHF and COPD. They were also more likely to abuse alcohol and nicotine, and have poor functional status. Serum albumin, hematocrit, and platelet counts were lower—and prothrombin time was higher—as renal function worsened.

There were 373 (1.8%) neurologic complications in all. The rate of stroke or coma was 1.7% in patients with normal or mildly depressed renal function, 1.9% in those with moderate CRI, and 2.7% in those with severe CRI. Although initially appearing to be higher in the severe CRI group, these differences were not statistically significant on bivariate (Table II) or multivariate (Fig, Table III) analysis. Significant risk factors included diabetes, either controlled by oral medications (odds ratio [OR], 1.3; 95% confidence interval [CI], 1.0-1.7; $P = .04$) or insulin (OR, 1.5; 95%

Table III. Multivariate analysis of postoperative complications and death by renal function category

Complication	*AOR*[a]	*95% CI*	P
GFR ≥60[b]	Ref	Ref	Ref
Neurologic			
GFR 30-59	1.1	0.8-1.3	.652
GFR <30	1.5	0.9-2.6	.124
Cardiac			
GFR 30-59	1.6	1.1-2.3	.009
GFR <30	0.6	0.2-2.1	.458
Pulmonary			
GFR 30-59	1.3	1.0-1.7	.031
GFR <30	1.6	0.9-2.9	.105
Infectious			
GFR 30-59	0.9	0.7-1.2	.664
GFR <30	1.9	1.0-4.0	.068
Death			
GFR 30-59	1.2	0.9-1.7	.269
GFR <30	2.7	1.6-4.8	<.001

AOR, Adjusted odds ratio; *CI,* confidence interval; *GFR,* glomerular filtration rate.
[a]Relative to a value of 1.00 for reference category with [b]estimated GFR ≥60 mL/min/1.73m^2.

Table IV. Analysis of negative outcomes risk based on presence of preoperative neurologic symptoms (stroke or transient ischemic attack before carotid endarterectomy)

Complication	*Asymptomatic, %*	*Symptomatic, %*	*Overall, %*
Univariate analysis			
Neurologic	1.1	2.4[a]	1.8
Cardiac	1.1	1.3	1.2
Pulmonary	1.1	2.0[a]	1.5
Infectious	1.4	2.3[a]	1.8
Death ≤30 days	0.8	1.6[a]	1.2
	AOR[b]	*95% CI*	P
Multivariate analysis			
Neurologic	2.1	1.6-2.6	<.001
Cardiac	. . .	. . .	NS
Pulmonary	1.6	1.1-2.4	.023
Infectious	1.6	1.3-2.1	<.001
Death ≤30 days	1.6	1.1-2.3	.006

AOR, Adjusted odds ratio; *CI,* confidence interval.
[a]$P < .001$, χ^2.
[b]Results of multivariate analysis estimating increased risk in the symptomatic group versus the asymptomatic group as the reference.

CI, 1.0-2.1; $P = .04$), history of TIA (OR, 1.9; 95% CI, 1.5-2.3; $P < .001$), previous stroke (OR, 1.9; 95% CI, 1.5-2.4; $P < .001$), and dependent functional status (OR, 1.8; 95% CI, 1.3-2.4; $P < .001$).

A total of 245 patients (1.2%) experienced a postoperative cardiac complication. Cardiac occurrences were almost twice as frequent in the moderate CRI group than in the control group (1.7% vs 0.9%), which was statistically significant ($P < .001$). After the multivariate analysis was adjusted for the other significant risk factors, moderate CRI remained predictive. In the multivariate model, the adjusted OR (AOR) was 1.6 (95% CI, 1.1-2.3; $P = .009$). The rate of cardiac complications in the severe CRI group was 1.0%, which was not significantly different than in the control group.

Pulmonary complications (324, 1.5% overall) were more frequent in groups with moderate CRI (2.1%, $P < .001$) and severe CRI (3.1%, $P < .001$) compared with the control group (1.3%). The use of general anesthesia, presence of diabetes mellitus, history of COPD, history of TIA or stroke, poor functional status, smoking, and ASA class 4 were also significantly associated with increased pulmonary complications on bivariate analysis. After adjustment in the multivariate model, moderate CRI (GFR 30-59 mL/min/1.73 m^2) was independently predictive (AOR, 1.3; 95% CI, 1.0-1.7; $P = .031$), but severe CRI was not.

There were 384 (1.8%) infectious complications, of which there was a graduated association with worsening renal function (GFR ≥60 mL/min/1.73 m^2, 1.5%; GFR 30-59 mL/min/1.73 m^2, 2.4%; and GFR <30 mL/min/1.73 m^2, 4.5%; $P < .001$). Older age and dependent functional status were also significant on bivariate analysis; however, after adjustment, these two factors alone were predictive in the multivariate model but degree of CRI was not.

Overall, 249 patients (1.2%) died within 30 days of CEA. In the control group, operative mortality was 1.0%, consistent with previous reports. The risk was significantly increased in moderate CRI patients (1.4%, $P = .048$) and much higher in the severe CRI group (3.1%, $P < .001$). Other significant factors included history of stroke, CHF, poor functional status, ASA class ≥3, and WBC count >12,000 cells/mL. After adjusting for other risk factors, GFR <30 mL/min/1.73 m^2 remained independently predictive of death (AOR, 2.7; 95% CI, 1.6-4.8; $P < .001$), along with history of stroke, CHF, poor functional status, and ASA class ≥3.

Poorer outcomes in symptomatic vs asymptomatic carotid stenosis. About 50% (10,497) of the operations in our data set were performed in patients who had neurologic symptoms before CEA. Negative outcomes were almost twice as common in the symptomatic group than in the asymptomatic group across all categories except cardiac complications (Table IV). In the multivariate analysis, a history of stroke or TIA before CEA was an independent predictor of increased neurologic events (AOR, 2.1; 95% CI, 1.6-2.6; $P < .001$) and death (AOR, 1.6; 95% CI, 1.1-2.3; $P = .006$) after surgery. Moreover, the risks of infectious complications (AOR, 1.6; 95% CI, 1.0-2.1; $P < .001$) and pulmonary complications (AOR, 1.6; 95% CI, 1.0-2.1; $P = .023$) were clearly increased to a significant degree in symptomatic patients.

DISCUSSION

Several attempts have been undertaken to investigate the relationship between CEA outcomes and renal function, but most have been limited, single-institution reports with relatively small sample sizes, have used serum creatinine concentration as a cutoff, and have had conflicting results. Debing et al[19] examined 102 patients labeled as having CRI (defined as creatinine ≥1.5 mg/dL and creatinine clearance ≤30 mL/min) vs 909 healthy patients, finding a significantly higher mortality in the CRI group (3.9% vs 1.0%). Likewise, Ascher et al[18] compared 166 patients with renal disease vs 443 healthy subjects and demonstrated no differences in stroke rate. They did see a higher mortality rate in those whose creatinine >3.0 mg/dL, but not necessarily when creatinine was between 1.5 and 2.9 mg/dL. Tarakji et al[20] examined 143 patients with CRI out of 1351 consecutive CEAs. Normal function, moderate CRI, and severe CRI were defined by creatinine cutoffs at 1.5 and 3.0 mg/dL. Compared with 150 healthy patients, they found a markedly increased rate of stroke, myocardial infarction, and death as renal function worsened.

Conversely, Reed et al[10] did a retrospective review of 1370 consecutive CEAs and defined renal insufficiency as a creatinine level >2.0 mg/dL. They found no differences in stroke rate at all, and no higher risk of death attributable to renal function alone. The mortality rate was only increased in patients who had two or more defined risk factors, such as CHF, COPD, contralateral carotid occlusion, or recent coronary artery bypass graft surgery. Reil et al[21] examined 370 CEAs performed by a single surgeon. They defined CRI as creatinine >1.5 mg/dL and demonstrated no difference in stroke or death rates.

The greatest limitation to studies like these is that serum creatinine levels alone are a late and inadequate marker of total renal function[27] for three main reasons.

First, creatinine is freely filtered by the glomerulus, but is also secreted by the proximal tubule. Thus, excretion into urine is a combination of both filtered and secreted creatinine rather than filtered alone, erroneously increasing creatinine clearance and systematically overestimating the GFR. This overestimation ranges from 10% to 40% in healthy individuals, and can be higher and less predictable in those with chronic kidney disease.[22]

Second, creatinine metabolism is variable, depending on many factors such as age, sex, and race.[28] The generation of creatinine depends on factors like lean muscle mass and dietary meat or protein intake, whereas the excretion of creatinine can occur extrarenally through degradation by bacterial overgrowth in the small bowel. It has been estimated that in patients with chronic kidney disease, as much as two-thirds of the total daily creatinine excretion occurs extrarenally.[23] As a consequence, up to 40% of those with a decreased GFR can still have serum creatinine levels within the normal range for a particular laboratory.

Third, the measurement itself of serum creatinine is subject to artifact and interference, depending on particular assays that differ among various laboratories.[29] This will overestimate or underestimate the GFR, depending on the enzymatic and analytic methods used at different institutions.

In our study, 13,965 patients with adequate (normal or mildly reduced) renal function (GFR ≥60 mL/min/1.73 m^2 as the cutoff) were compared with 6423 patients with moderate CRI (GFR 30-59 mL/min/1.73 m^2) and 511 patients with severe CRI (GFR <30 mL/min/1.73 m^2) but without dependence on dialysis. We did not detect any statistically significant associations between renal function and the development of postoperative neurologic complications, but there was a trend toward increasing risk with a worsening GFR (Fig).

Because the VA-NSQIP is not a vascular surgery registry, technical aspects of CEA—such as contralateral carotid artery occlusion, operative technique, or use of patching—that may have an effect on the rate of neurologic complications could not be analyzed. Interestingly, contrary to other studies that have shown no effect on stroke rate from diabetes mellitus,[30] we found adverse neurologic outcomes were significantly higher in diabetic patients. Even adjusting for other factors, diabetic patients taking oral medications (AOR, 1.3; 95% CI, 1.0-1.7; $P = .04$) or requiring insulin (AOR, 1.5; 95% CI, 1.0-2.1; $P = .04$) were at increased risk. Other independent risk factors for neurologic complications were history of TIA (AOR, 1.9; 95% CI, 1.5-2.3; $P < .001$) and stroke (AOR, 1.9; 95% CI, 1.5-2.4; $P < .001$), which we had used to identify symptomatic patients.

Defining patients with symptomatic carotid disease has been historically inconsistent. NASCET included only patients with hemispheric TIA, amaurosis fugax, or nondisabling stroke ≤120 days, and excluded those who experienced cerebral infarction that had eliminated useful function in the affected arterial territory.[3] ESCT included any patient with a carotid lesion who had at least one transient or mild ischemic vascular event in the distribution of one or both carotid arteries within the previous 6 months.[4] By definition, all of the patients in our study had a carotid lesion amenable to operation. Thus, we considered any patient with history of stroke or TIA preoperatively to have symptomatic carotid disease. Almost exactly half of the 20,899 subjects were symptomatic, allowing for good statistical comparisons between the two groups. Symptomatic patients had strikingly increased operative morbidity, higher rates of postoperative neurologic complication, and a greatly increased mortality rate (Table IV).

We were able to demonstrate clearly that moderate CRI is an independent predictor of increased cardiac and pulmonary complications, but not 30-day mortality or neurologic complications. On the other hand, increased cardiopulmonary or neurologic morbidity was not discovered in those with severe CRI, but mortality was markedly increased in this group (AOR, 2.7). Given the small relative proportion of subjects comprising the severe CRI group (2.4%), the increased mortality rate may explain why additional complications did not develop, and thus, why statistical significance was not reached in the severe CRI group. Other independent risk factors for cardiac complications included history of CHF and poor functional status.

Pulmonary complications were independently predicted by moderate CRI, as well as diabetes mellitus, history of COPD, smoking, ASA class 4, poor functional status, and the use of general anesthesia. It is important and interesting to note that only the patients with severe CRI

Table V. Percentage of patients experiencing adverse outcomes after carotid endarterectomy, adjusting for risk factors[a]

	GFR >60							
	Functionally independent				*Needs assistance*			
	Neuro symptoms absent		*Neuro symptoms present*		*Neuro symptoms absent*		*Neuro symptoms present*	
Complication	*D− 5057*	*D+ 1723*	*D− 4738*	*D+ 1528*	*D− 130*	*D+ 76*	*D− 480*	*D+ 232*
Neuro	1.0	1.6	1.7	2.9	1.5	1.3	5.0	4.7
Cardiac	0.6	1.5	0.8	1.1	1.5	1.3	2.5	1.7
Pulmonary	0.7	1.3	1.4	1.8	2.3	1.3	1.5	6.0
Infectious	0.9	1.3	1.5	2.0	0.8	1.3	4.2	6.9
Death	0.6	0.8	1.1	1.6	2.3	4.0	3.1	3.5
Any	2.9	4.4	4.5	6.4	4.6	6.6	10.4	13.4

GFR, Glomerular filtration rate (mL/min/1.73m^2) as defined by the Modification of Diet in Renal Disease formula (see Methods); *Functionally independent,* patient does not require nursing care or assistant devices for bathing, feeding, toileting, dressing, or walking in the previous 30 days; *Neuro symptoms,* preoperative TIA or stroke; *D+,* oral medications or insulin for diabetes mellitus; *D−,* does not require oral medications or insulin for diabetes mellitus.
[a]This table describes the percentage of patients who experienced an adverse outcome after undergoing carotid endarterectomy. Four risk factors that were statistically significant in at least two of the multivariate regression analyses for the outcomes listed were selected. To use this table, determine the risk factors of interest and then locate the appropriate column. The number at the top of each column indicates the number of patients in the cohort meeting these criteria. The number in each row next to an outcome is a percentage. For example, patients with a GFR of 30 to 59, functional independence, no neurologic symptoms, and diabetes mellitus (n = 859) experienced a cardiac outcome in 2.1% of cases and death in 1.5% of cases.

(GFR <30 mL/min/1.73 m^2) were statistically more likely to have been given regional rather than general anesthesia ($P = .03$) at the discretion of the surgeons and anesthesia providers. This effect, along with the higher mortality rate that was cited, may also help explain why increased pulmonary complications were not recorded as often in those with severe CRI compared with the control group. This implication that anesthesia type may influence pulmonary outcomes to a greater degree than renal function after CEA deserves further investigation.

In the development of infectious complications, worsening renal function showed graduated bivariate relationships, with higher incidences as GFR decreased. However, these were no longer significant after adjustment in the multivariate model, suggesting a correlation with other predictive risk factors such as age and functional status.

There were 249 deaths within 30 days, yielding an operative mortality of 1.2%. The odds were significantly higher in both the moderate CRI and severe CRI groups on bivariate analysis, but after adjustment, only GFR <30 mL/min/1.73 m^2 remained independently predictive (AOR, 2.7; 95% CI, 1.6-4.8; $P < .001$). The effect is profound, almost independently tripling the odds of death after CEA. This confirms the findings of other recently published studies examining renal function and operative outcomes, when stratified by GFR. Estrera et al[31] showed that preoperative CRI defined by GFR was the most significant predictor of death during repairs of the ascending and transverse aortic arch. In a meta-analysis of 31 studies, Mathew et al[32] found that patients with chronic kidney disease had higher rates of cardiovascular complications and death in elective noncardiac operations. Their multivariate analysis of renal dysfunction revealed a strong, independent, graded relationship between severity of renal disease (declining GFR) and mortality rates.

To permit the reader to determine the risk of worsening GFR in conjunction with other risk factors, we constructed Table V using the four risk factors that were statistically significant in more than one multivariate regression analysis (eg, pulmonary complications and death). (History of CHF was significantly associated with cardiac complications and death, but was excluded from Table V for simplicity.) By examining renal function (by GFR), functional status (by independence versus need of assistance), preoperative neurologic symptoms (stroke or TIA), and presence of diabetes mellitus, Table V provides the reader with the percentage of patients in the cohort who had an adverse outcome for any combination of risk factors. These data could be used to provide an estimate of risk for an individual patient or to allow surgeons or groups of surgeons to evaluate their rates of complications against this large cohort with appropriate adjustment for case-mix. Of course, all of the patients in this study were determined to be surgical candidates, and there was no comparison with medical therapy vs surgery. It would be inappropriate to use the data from Table V in isolation of these considerations.

CONCLUSION

We have found that CRI, defined by GFR, significantly affects outcomes after CEA. Though impaired renal function alone is not a risk factor for neurologic or infectious complications, moderate CRI (GFR 30-59 mL/min/1.73 m^2) independently increases the risk of cardiac and pulmonary complications, but not death. The operative mortality rate is much higher in those with severe CRI (GFR <30 mL/min/1.73 m^2) compared with those with adequate renal function. Chronic renal insufficiency should be considered an independent risk factor for this operation, and these patients should be carefully evaluated before CEA to optimize existing cardiac and pulmonary disease. Under-

Table V. Continued

GFR 30-59								GFR <30	
Functionally independent				*Needs assistance*					
Neuro symptoms absent		*Neuro symptoms present*		*Neuro symptoms absent*		*Neuro symptoms present*		*Functionally independent*	*Needs assistance*
D− 2202	*D+ 891*	*D− 1997*	*D+ 877*	*D− 66*	*D+ 59*	*D− 192*	*D+ 138*	*466*	*45*
1.2	0.7	2.3	3.1	1.0	1.7	2.1	5.8	1.9	11.1
1.1	2.1	1.4	2.1	6.1	1.7	4.2	5.8	0.6	4.4
1.0	2.5	1.9	3.4	1.5	1.7	4.2	8.7	2.6	8.9
2.0	1.6	2.2	3.2	1.5	5.1	6.8	6.5	4.3	6.7
0.6	1.5	1.5	1.9	1.5	3.4	2.1	5.1	2.8	6.7
4.1	5.7	6.7	9.0	7.6	11.9	11.5	13.8	8.8	22.2

standing this increased risk may assist the surgeon in preoperative counseling and perioperative management.

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AUTHOR CONTRIBUTIONS

Conception and design: AS, PW
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Data collection: AS, GA, PW, WH
Writing the article: GA, OJ
Critical revision of the article: AS, OJ, PW, KD
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